

§Appl. No. 09/965,807  
Amdt. dated December 2, 2004  
Reply to Office Action of, July 2, 2004

**Listing of Claims:**

Please amend the claims as follows:

**Claim 1      (Cancelled)**

**Claim 2      (Cancelled)**

**Claim 3      (Cancelled)**

**Claim 4      (Cancelled)**

**Claim 5      (Cancelled)**

**Claim 6      (Cancelled)**

**Claim 7      (Cancelled)**

**Claim 8      (Cancelled)**

**Claim 9      (Cancelled)**

**Claim 10      (Cancelled)**

**Claim 11      (Cancelled)**

**Claim 12      (Cancelled)**

**Claim 13      (Cancelled)**

**Claim 14      (Cancelled)**

**Claim 15      (Cancelled)**

**Claim 16      (Cancelled)**

**Claim 17      (Cancelled)**

**Claim 18      (Cancelled)**

**Claim 19      (Cancelled)**

**Claim 20      (Cancelled)**

**Claim 21      (Cancelled)**

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**Claim 22 (Currently Amended)** An isolated naturally-occurring mutant human aspartoacylase polypeptide ~~which~~ having either an altered ability to hydrolyze N-acetyl-aspartic acid to aspartate and acetate, as compared with a normal wild-type human aspartoacylase, or incapable of hydrolyzing N-acetyl-aspartic acid to aspartate and acetate, and having comprising the amino acid sequence SEQ ID NO: 2 of wild-type human aspartoacylase, except for said mutation, which is

E285 > A,

Y231 > X, and/or

A305 > E,

or an allelic variant of said mutant aspartoacylase a naturally-occurring mutant allele of said wild-type human aspartoacylase.

**Claim 23 (Cancelled)**

**Claim 24 (Previously Presented)** A mutant aspartoacylase of claim 22, wherein the glutamic acid at amino acid position 285 is substituted by alanine.

**Claim 25 (Cancelled)**

**Claim 26 (Cancelled)**

**Claim 27 (Cancelled)**

**Claim 28 (Cancelled)**

**Claim 29 (Cancelled)**

**Claim 30 (Cancelled)**

**Claim 31 (Cancelled)**

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**Claim 32 (Cancelled)**

**Claim 33 (Cancelled)**

**Claim 34 (Cancelled)**

**Claim 35 (Cancelled)**

**Claim 36 (Cancelled)**

**Claim 37 (Cancelled)**

**Claim 38 (Cancelled)**

**Claim 39 (Cancelled)**

**Claim 40 (Cancelled)**

**Claim 41 (Cancelled)**

**Claim 42 (Cancelled)**

**Claim 43 (Cancelled)**

**Claim 44 (Cancelled)**

**Claim 45 (Cancelled)**

**Claim 46 (Cancelled)**

**Claim 47 (Cancelled)**

**Claim 48 (Cancelled)**

**Claim 49 (Cancelled)**

**Claim 50 (Cancelled)**

**Claim 51 (Cancelled)**

**Claim 52 (Cancelled)**

**Claim 53 (Cancelled)**

**Claim 54 (Cancelled)**

**Claim 55 (Cancelled)**

**Claim 56 (Cancelled)**

**Claim 57 (Cancelled)**

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**Claim 58** (Cancelled)

**Claim 59** (Cancelled)

**Claim 60** (Cancelled)

**Claim 61** (Cancelled)

**Claim 62** (Cancelled)

**Claim 63** (Previously Presented) A transgenic mouse exhibiting Canavan disease symptoms.

**Claim 64** (Cancelled)

**Claim 65** (Cancelled)

**Claim 66** (Currently Amended) A fragment of a mutant human aspartoacylase of claim 22, comprising an aspartoacylase epitope which is immunologically-effective to elicit antibodies that selectively bind to said human aspartoacylase.

**Claim 67** (Currently Amended) A recombinant normal wild-type human aspartoacylase capable of hydrolyzing N-acetyl aspartic acid to aspartate and acetate, having comprising an amino acid sequence which has a sequence identity of at least 95% to the sequence of SEQ ID NO: 2.

**Claim 68** (Currently Amended) A fragment of a recombinant normal wild-type human

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aspartoacylase of claim 20 67, comprising an aspartoacylase epitope which is immunologically-effective to elicit antibodies that selectively bind to said human aspartoacylase.

**Claim 69 (Currently Amended)** A pharmaceutical composition, comprising an isolated normal wild-type human aspartoacylase having comprising the amino acid sequence SEQ ID NO: 2, or a naturally-occurring polymorphic form thereof, and a pharmaceutically acceptable carrier.

**Claim 70 (Currently Amended)** An isolated normal human aspartoacylase having comprising the amino acid sequence SEQ ID NO: 2, or a naturally-occurring polymorphic form thereof, which is free of other cellular components.

**Claim 71 (Currently Amended)** An isolated normal normal-type human aspartoacylase having comprising the amino acid sequence SEQ ID NO: 2, or a naturally-occurring polymorphic form thereof, which is free of other human proteins.

**Claim 72 (Currently Amended)** A preparation which consists essentially of a normal wild-type human aspartoacylase having comprising the amino acid sequence SEQ ID NO: 2, or a naturally-occurring polymorphic form thereof.

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**Claim 73 (Currently Amended)** An isolated normal wild-type human aspartoacylase having comprising the amino acid sequence SEQ ID NO: 2, or a naturally-comprising polymorphic form thereof, in a concentration which can be administered to a patient at a dosage of 0.1 to 100 U/kg.

**Claim 74 (Currently Amended)** A normal wild-type human aspartoacylase having comprising the amino acid sequence SEQ ID NO: 2, or a naturally-occurring polymorphic form thereof, produced by

- (a) culturing a host cell transformed with a vector comprising a DNA which encodes for a normal human aspartoacylase of claim 20 80 in a cell culture medium under conditions whereby the aspartoacylase is expressed, and
- (b) isolating the thus-produced normal wild-type aspartoacylase.

**Claim 75 (Currently Amended)** A normal wild-type human aspartoacylase having comprising the amino acid sequence SEQ ID NO: 2, or a naturally-occurring polymorphic form thereof, produced in a bacterium, a fungus, or a non-human mammalian cell.

**Claim 76 (Withdrawn)** An immunologically active anti-aspartoacylase polyclonal or monoclonal antibody specific for an aspartoacylase polypeptide of claim 20.

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**Claim 77** **(Withdrawn)** An immunologically active anti-aspartoacylase polyclonal or monoclonal antibody specific for an aspartoacylase polypeptide of claim 22.

**Claim 78** **(Withdrawn)** A hybridoma producing a moloclonal antibody specific for an aspartoacylase polypeptide of claim 20.

**Claim 79** **(Withdrawn)** A hybridoma producing a moloclonal antibody specific for an aspartoacylase polypeptide of claim 22.

**Claim 80** **(Currently Amended)** A recombinant normal wild-type human aspartoacylase capable of hydrolyzing N-acetyl aspartic acid to aspartate and acetate, having comprising the amino acid sequence SEQ ID NO: 2, or a naturally-occurring polymorphic form thereof.

**Claim 81** **(Currently Amended)** A normal wild-type human aspartoacylase polypeptide purified to homogeneity and capable of hydrolyzing N-acetyl-aspartic acid to aspartate and acetate.

**Claim 82** **(Previously Presented)** The aspartoacylase of claim 81 having SEQ ID NO: 2.

**Claim 83** **(New)** An isolated polypeptide of claim 22 which is encoded by a nucleic acid

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which specifically hybridizes under stringent conditions to a nucleotide sequence of SEQ ID NO:1.

**Claim 84 (New)** An isolated polypeptide of claim 66 which is encoded by a nucleic acid which specifically hybridizes under stringent conditions to a nucleotide sequence of SEQ ID NO:1.

**Claim 85 (New)** An isolated polypeptide of claim 67 which is encoded by a nucleic acid which specifically hybridizes under stringent conditions to a nucleotide sequence of SEQ ID NO:1.

**Claim 86 (New)** An isolated polypeptide of claim 68 which is encoded by a nucleic acid which specifically hybridizes under stringent conditions to a nucleotide sequence of SEQ ID NO:1.

**Claim 87 (New)** An isolated polypeptide of claim 71 which is encoded by a nucleic acid which specifically hybridizes under stringent conditions to a nucleotide sequence of SEQ ID NO:1.

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**Claim 88 (New)** An isolated polypeptide of claim 72 which is encoded by a nucleic acid which specifically hybridizes under stringent conditions to a nucleotide sequence of SEQ ID NO:1.